HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Protocol Title:	**A5314 FINAL Version 1.0, dated 7/11/13; Letter of Amendment, 11/25/13; Letter of Amendment #2, 8/6/14** Effect of Reducing Inflammation with Low Dose Methotrexate on Inflammatory Markers and Endothelial Function in Treated and Suppressed HIV Infection
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Introduction:

You are being asked to take part in this research study because you are infected with human immunodeficiency virus (HIV), the virus that causes AIDS, have been taking anti-HIV medicines for at least 6 months, your viral load level is under control, and you either have cardiovascular disease (heart disease) or you are at higher risk for cardiovascular disease (CVD). This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is: Dr. Pablo Tebas. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?

Inflammation is the body's normal reaction to any infection. HIV-infected people can have an increase in inflammation in their body organs, even after taking anti-HIV medicines. Also, HIV-infected people who are doing well on anti-HIV medications have a higher risk of getting certain medical conditions, including heart disease. If inflammation lasts a long time as it does in HIV infection, it may lead to other health problems, such as heart disease and stroke. Many HIV researchers are studying the harmful effects of this long-term inflammation and possible ways to prevent these complications.

We are doing this study to learn more about the effects of low dose methotrexate (LDMTX) on inflammation and cardiovascular (heart) health. LDMTX is a medication used to treat inflammation, and has been used safely in people with rheumatoid arthritis (a type of arthritis with joint inflammation) for over 20 years in the US. LDMTX is approved by the US Food and Drug Administration (FDA) for treating people with rheumatoid arthritis.

LDMTX is being used in this study to control inflammation associated with HIV infection; it is not approved for the treatment of HIV infection. We want to learn if treatment with LDMTX can lower the risk of heart disease by lowering HIV-related inflammation. This will be done by a test that uses an ultrasound to measure the flow of blood in your arm, called flow-mediated vasodilation (FMD) of the brachial artery. This is a painless test that bounces sound waves off of a blood vessel in your arm. We also want to see how safe LDMTX is when used in people with treated HIV infection.

How Many People Will Take Part in This Study?
About 200 men and women 40 years of age and older will take part in this study. About 5-7 are expected to enroll at the University of Pennsylvania.

How Long Will I Be In This Study?
You will be in this study for about 36 weeks or 9 months.

What Do I Have To Do If I Am In This Study?
If you decide to join this study, you will continue taking your current anti-HIV drugs. You will be randomized by chance (like the flip of a coin) to get either LDMTX or placebo (a placebo is a pill that does not have any active medicine) along with folic acid (a B-vitamin), as shown below. Folic acid is used to protect your liver from possible side effects of LDMTX. These side effects are seen in people taking much higher doses of MTX than the dose you will take. You will take LDMTX or the placebo on the same day once each week and folic acid every day until you reach week 24 of the study. Depending on the results of the laboratory tests, the LDMTX and placebo dose may be increased after week 1 and/or week 12, as shown below. If it is safe for you to increase your dose, the staff and your site will contact you by telephone and give you directions on how to take your medicine, including the number of pills to begin taking.

Study Visits	Active Drug		Matching Placebo
From entry through week 1	LDMTX (5 mg/week) + folic acid (1 mg/day) by mouth		placebo (once weekly)+ folic acid (1 mg/day) by mouth
After week 1 visit through week 12	LDMTX (10 mg/week) + folic acid (1 mg/day) by mouth	OR	placebo (once weekly) + folic acid (1 mg/day) by mouth
After week 12 visit through week 24	LDMTX (15 mg/week) + folic acid (1 mg/day) by mouth		placebo (once weekly)+ folic acid (1 mg/day) by mouth
Week 24 visit through week 36 visit	No study treatment – continue study follow-up		

This is a double-blind study, which means neither you nor the study staff will know whether you will get the active drug or placebo. You have an equal chance of getting the active drug (LDMTX) or the matching placebo but neither you nor the study staff will be able to decide which you will get. LDMTX, placebo, and folic acid are given to you for free by the study. Anti-HIV drugs will not be provided by the study.

While you are in this study, you will need to be seen in the clinic about 10 times during the 36 weeks of the study. The study staff will tell you about how long each visit could be. You may need to come to the clinic if you have side effects or if you switch or take new anti-HIV drugs. More information about the study tests is given below. During the study, you will get the results from any routine tests that are done during the study when they are available.

You must fast for the screening, pre-entry, entry, weeks 12 and 24, and early treatment/study discontinuation visits. (Fasting means that you should not eat or drink anything for at least 8 hours before your visit. You may only drink water and take your prescription medications during this time). The study staff will remind you to fast before each of these study visits. You must also avoid exercising and smoking for at least 8 hours before the visits when the arm ultrasound tests will be done. If you do not fast before these visits and avoid smoking and exercising at least 8 hours before your visit, you will be asked to come back later for these tests after you have met these conditions.

If you do not enroll into the study

If you decide not to take part in this study or if you do not qualify to take part in this study, we will still use some of your information. As part of the screening visit, some demographic (for example, age, gender, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, CD4+ T-cell count, viral load) information is being collected from you so that ACTG (AIDS Clinical Trials Group) researchers may see if there are patterns or common reasons why people do not join a study. If you do not want this information to be recorded, you should not sign this consent form and not participate in the study. If you elect not to participate, all information collected thus far by the research team will be destroyed.

Required Tests

Some of your blood will be stored (with no information that will identify you) and used for testing your immune cells, HIV, hepatitis and herpes viruses, RNA and DNA, and tests that show how your body uses food. These tests are required for this study.

Optional Tests

If you agree, any blood leftover after all required study testing is done may be stored (with no information that will identify you) and used for future ACTG-approved HIV-related research. These blood samples may be stored for an unknown period of time. Results of testing done on these samples may not be given to you.

A5314 Study Visits

The study staff can answer any questions you have about individual study visits, the evaluations that will occur, or how long each visit will be. The table below can be used as a quick reference for you, along with the explanations that follow.

I. Study Schedule

Evaluation or test	Screening (fasting)	Pre-Entry (fasting)	Entry (fasting)	Post-Entry Visits		Other visits	Early discontinuation
				Most Visits	Some Visits		
Consent	✓						
Physical exam	✓		✓	✓			✓
Blood collected	✓		✓	✓		✓	✓
Pharmacokinetic (PK) sample[1]					At week 2		
Arm ultrasound tests (FMDs)		(done twice)			At weeks 12 & 24 (done once at each visit)		✓
Adherence assessments			✓	✓			✓

[1] Taking part in the PK sample collection is optional but strongly encouraged

II. Description of Study Visits

Screening

After you have read and signed the consent form, you will have several tests, including blood being taken, to make sure that you qualify to join the study. You must come to the visit fasting. If you are not fasting within the past 8 hours before this visit, you will be asked to come back fasting. Some of the blood taken will be shipped to a testing lab. You will have a chest X-ray before starting in the study. You may be asked to get a skin test to make sure that you do not have inactive tuberculosis (TB) before starting in the study. If the test is positive, you will not qualify for this study. If you are a woman and are able to become pregnant, you will not qualify for this study. If you are a postmenopausal woman and do not have documentation of your postmenopausal status, you will have additional tests to document your status.

Pre-entry

You must come in fasting. If you are not fasting or have exercised or smoked within the past 8 hours before this visit, you will be asked to come back later for these tests after you have met these conditions.

The ultrasound on the arm will be done twice at the pre-entry visit. The test may be done on the same day or within 3 days before starting study drugs.

Entry

When all of the results from your screening tests are available you will come back to the clinic to begin the study. You must come in fasting. If you are not fasting or have exercised or smoked within the past 8 hours before this visit, you will be asked to come back later to repeat some blood tests after you have met these conditions.

At this visit, you will get your study drugs.

Post-entry visits
You will be seen at weeks 1, 2, 4, 8, 12, 18, 24, and 36 after starting the study drugs. These visits will last about 1-1 ½ hours each.

Some subjects who are taking tenofovir (Truvada, TFV, TDF) to treat their HIV may have an extra evaluation (PK sample) done at the Week 2 study visit. This extra evaluation is optional, described below. The staff at your site will tell you before you start the study if this evaluation will be required.

Other visits
During the study, you may have to come back to the clinic for extra visits for testing of any lab results that are not normal, or to follow-up on a specific side effect or symptom.

Early discontinuation
There are two types of discontinuation (stopping study treatment or leaving the study early) in which you will be asked to come to the clinic for an extra visit:

1. Stop study treatment early
   You or your doctor may decide to stop the study medication that you began at entry.

   If you must stop taking the study medication before week 24, the study doctor may ask you to stay in the study and come in for some study visits and tests.
2. Leave study early
   You or your doctor decide that you will no longer stay in the study or you are notified the study is stopped early.

III. Description of Study Evaluations

Consent
After you read the consent and have had a chance to ask questions about the study, you will sign the consent form if you want to continue to be tested to see if you qualify for the study.

Physical examination
You will have a physical exam. The study staff will check the different systems in your body such as heart, abdomen, lower body, skin, head, mouth, neck, and head. The study staff will also check your vital signs such as temperature, blood pressure, pulse, and respiratory rate. You will be asked questions about your health and about any medicines you have taken or are taking now.

Blood collection and samples
Blood will be taken from a vein in your arm for different tests during the study. Approximately 130 mL (9 tablespoons) of blood will be drawn during any study visit. These include routine safety tests at every visit. Blood will be drawn and stored for immune system testing that is required for this study; these tests will look at how your body fights against illness and its reaction to the study treatment. HIV viral load (a test that shows how much HIV is in your blood), CD4+ T-cell count (a test that shows how many infection-fighting cells you have in your blood), and hepatitis testing will also be done.

Hormonal tests (as needed)
If you are a woman and do not have documentation of your postmenopausal status or removal of your ovaries, you will have blood taken for testing.

Optional Blood sample PK (for some subjects only)
If you are taking tenofovir (TFV) and you are one of about 21 evaluable subjects enrolled in a group (active drug or placebo and participating in the PK part, , you will have blood collected six times (for a total of approximately 2 tablespoons) during a 6-hour PK sampling period. The PK samples will be used to measure the levels of the study drugs in your blood since there is currently no information available about the interaction between tenofovir and the study drugs. You may be given breakfast to eat in the clinic on the morning of your PK visit. You will not take your study medications that morning until you arrive at the clinic and are instructed to do so. You may also be given additional instructions as to whether you will need to change the dosing schedule of your HIV medications. Your visit will last 6 hours. ,

If you are scheduled to have a PK sample drawn, you will be given a medication diary to write down when you take your last 4 doses of HIV medications before the PK visit.

NOTE: If you are unable to complete the PK sample collection, you will remain in the study until the final visit.

Arm ultrasound tests (FMDs)
You will be asked to fast, to not smoke cigarettes, and to not exercise for 8 hours before this test. This test bounces sound waves off of a blood vessel in your arm to see how it reacts to changes in blood flow. This is a safe, painless test that is done while you lie comfortably on a special table. You will be asked to lie back on the exam table and a blood pressure cuff will be put on your arm to check your blood pressure and heart rate during the test. A small amount of gel will be put on the outside part of your right arm and the ultrasound transducer (probe) will be put over your arm to get a picture of the brachial artery. The transducer will be moved to get the best picture which will then be recorded on the machine to be checked later. A blood pressure cuff will be put on your other arm and pumped up with air for 5 minutes and then let down. The transducer will be used to look at your arm again. The whole test takes about 30 minutes. If we are unable to do the ultrasound on the day you do the blood collection for the study, you may have to come another day for the ultrasound.

Adherence Assessments
You will be asked about how well you take your medications. The study staff will give you information and encouragement to help you take your medications as prescribed.

Why Would The Doctor Take Me Off This Study Early?

The study doctor may need to take you off the study early without your permission if:

- the study is cancelled
- a Safety Monitoring Committee (SMC) recommends that the study be stopped early (A SMC is an outside group of experts who monitor the study.)
- you are not able to come for the study visits as required by the study
- you are not able to take the study medications as required by the study
- your doctor thinks the study is no longer in your best interest

The study doctor may also need to take you off the study drugs without your permission if:

- continuing the study drugs may be harmful to you
- you need a medication that you may not take while on the study

If I have to permanently stop taking LDMTX through the study, or once I leave the study, how can I get LDMTX?

If you must permanently stop taking LDMTX before the study is over, the study staff will talk with you about other options.

After you have finished the study, you will not be able to get LDMTX through the study.

What Are The Risks Of The Study?

The drugs used in this study may have side effects, some of which are listed below. These lists do not include all the side effects seen with these drugs. These lists include the more serious or common side effects that are known or may be caused by the study drugs. If you have questions about other study drug side effects please ask the study staff.

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study drugs. For your safety, you must tell the study staff about all medications you are taking before you start the study and also before starting any new medications while on the study. This includes non-prescription over-the-counter medications such as ibuprofen, the drug in Advil and Motrin and naproxen, the drug in Aleve. Also, you must tell the study staff before going into any other research studies while on this study.

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for side effects. Side effects may be mild or serious. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, long lasting, or may never go away. You should talk to the study staff about any side effects you have while taking part in the study.

The safety of MTX in patients with HIV infection is not known, so we are enrolling HIV-infected persons with undetectable HIV levels (too low for the lab to count them) and normal CD4+ (immune cell) counts. Side effects of MTX on HIV infection including HIV and CD4+ levels, and worsening of CMV (cytomegalovirus) disease will be watched closely during this study.

People taking MTX may have rare but possibly serious side effects. Higher doses of MTX - much higher than used in this study - can lead to liver problems. The folic acid we are giving you will help prevent this. Kidney problems can happen with high doses of MTX. High doses of MTX often lower blood cell counts. At the doses used in this study, lowering of blood cell counts is expected to be uncommon. In this study, we will do careful first-time and follow-up laboratory tests to watch for any signs of liver, kidney, or blood count problems.

Lung problems can happen with both high- and low-dose MTX and are most common with higher doses of MTX or if you already have lung disease. Your chest X-ray will be checked before you start this study.

Study Drugs	Risks/Side Effects
Methotrexate (MTX)	The major side effects of LDMTX include the following: Elevated liver tests and liver toxicity: This is most often seen in patients who already have liver disease such as active hepatitis B or active hepatitis C or who drink alcohol or who use MTX for a long period of time. This is why we are not allowing people into this study who have active hepatitis B or active hepatitis C or who drink on average 3 or more alcoholic beverages per day within the past 4 weeks (or who plan to drink more than 2 alcoholic beverages a day while on the study). Very mild increases in liver lab tests may happen sometimes (1 out of 5) but higher

Study Drugs	Risks/Side Effects
	increases in liver tests are uncommon (1 out of 100). Lung toxicity including fibrosis and interstitial pneumonitis: Lung toxicity has been seen with use of LDMTX. While it is unclear how often lung toxicity (problems) occur, a review of over 3400 patients taking MTX for rheumatoid arthritis found that lung problems were very uncommon- fewer than 1 out of 100 taking MTX. Lung problems most often occurred in people who already had lung disease or who were taking higher doses of MTX. Lung injury is uncommon at the doses used in this study. In most cases lung injury in patients on higher doses of MTX, the injury improved after stopping the drug. Low blood cell counts due to reduced bone marrow activity: Low blood cell counts are uncommon side effects (1.4 out of 100). This happens more often in people who already are at risk for low blood counts, who have abnormal kidney function, or who take MTX every day instead of weekly. Elevated kidney tests and kidney toxicity: This is very rare with long-term LDMTX use. In studies of high dose MTX, which is much higher than we are using in this study, the risk of kidney failure is very low (2 out of 100). Other common problems include stomach and intestinal problems including nausea, stomach upset, loose stools, inflammation in the mouth or mouth soreness, a rash, headache, tiredness, problems concentrating, hair falling out, fever, and abnormal blood tests. One or more of these side effects are seen at some time in most patients. They usually happen within 1-2 days after the weekly MTX dose. Use of MTX at higher doses can rarely be associated with the development of malignant lymphoma (a type of cancer); the lymphoma may shrink back after stopping treatment. If a lymphoma develops that does not resolve after MTX is stopped, treatment with cancer medications (“chemotherapy”) may be needed. Serious skin reactions and rashes are extremely rare but have been reported. If a rash occurs, you should stop the study medication and contact the study physician.
Folic Acid	The following side effects rarely happen with the use of high doses of folic acid – much higher than used in this study: • stomach cramps • diarrhea • rash • sleep problems • changes in behavior • stomach upset

Risks of randomization
You will be assigned by chance to either the LDMTX + folic acid or placebo + folic acid group. The medications you get may not work as well or may have more side effects compared to the other study treatment. This will not be known until the study is done and the study information has been analyzed.

If you are in the group that gets placebo, you will not take active drug, but you will take an inactive pill and continue to take your current anti-HIV medication regimen.

Risks of blood draws
A needle will be used to take blood from a vein in your arm. This may lead to brief pain from the needle stick, bruising, and rarely, infection. Some people become light-headed. The risk of taking blood includes low red blood cell counts, which can make you feel tired, weak, and dizzy. If the study staff feel you are at risk for low blood counts, the amount of blood taken will be lowered and your blood counts will be checked.

Risks of arm ultrasound tests (FMDs)
There may be mild but brief discomfort when the blood pressure cuff is inflated. You will be watched carefully during the entire test and it will be stopped if you have any problems.

Risks of Chest X-ray
This research study involves exposure to radiation from a chest x-ray. Therefore, you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

Unknown risks
Other side effects that are not known at this time could happen during the study. All drugs have a possible risk of an allergic reaction, which if not treated right away, could become life-threatening. During the study, you will be told about any new information that may affect your decision to stay in the study. If you decide to stay in the study, you will be asked to sign an updated consent form. If you decide to leave the study early, the study staff will talk with you about your treatment options.

Risks of test results
Getting test results may make you feel worried or nervous. Because some tests are experimental, test results cannot always be given to you. Laboratory results (for example, tests that check the fats in your blood) will be given to you after the study. However, the FMD (arm ultrasound) results and research blood tests will not be given to you. The FMD tests are done for research purposes only and the results of these tests will not change how your health is managed while on study.

Are There Risks Related To Pregnancy?

The effects of LDMTX on an unborn baby are harmful. MTX can cause a developing fetus to die or have severe birth defects. If you are woman who is breastfeeding, pregnant, or capable of becoming pregnant; you may not join this study. If you are a man who is having sex that could lead to pregnancy, you must agree not to make your partner pregnant.

NOTE: If you are not able to get pregnant or make your partner pregnant, the study staff will need to obtain documentation from your regular doctor. If documentation is available, you will not be asked to use birth control. If documentation is unavailable, men still may participate as long as they use birth control, the study staff will discuss options with you.

For Men
It is important to understand that you must use effective birth control. You and your partner must use at least two (2) forms of birth control while taking part in this study and for 90 days after your last dose of study drug. This is an extra caution to prevent pregnancy. Men and their partners may choose two or more of the birth control methods listed below:

- A condom (male or female) with or without a spermicide
- Diaphragm or cervical cap with spermicide
- An intrauterine device
- Tubal ligation
- Hormone-based contraceptives

You should inform your study doctor in case your partner becomes pregnant during the study. You should also inform your study doctor in case your partner becomes pregnant within 12 weeks after the final study visit or the last dose of study drugs.

You will be asked to provide information about your partner's pregnancy, her health status, and the outcome of her pregnancy. Also, the study staff will call you 6 months after delivery to ask how your baby is doing.

Are There Benefits to Taking Part in This Study?
If you take part in this study, it is possible that there will be no direct benefit to you. Your health may be watched more closely than usual while you are on the study, which may help you to feel better. It is also possible that you may get no benefit from being in this study. Information learned from this study may help others who have HIV.

What Other Choices Do I Have Besides This Study?
Study-provided drugs, laboratory tests to see how well these drugs are working, and good medical care may or may not be available to you outside the study. The study staff will discuss with you other treatment choices in your area and the risks and the benefits of all the choices.

What About Confidentiality?
We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, any publication of this study will not use your name or identify you personally. A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the web site will include a summary of the results. You can search this website at any time.

Your records may be reviewed by the AIDS Clinical Trials Group, Office for Human Research Protections (OHRP), Food and Drug Administration, the University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), study staff, study monitors, and other agencies supporting this study.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities.

Your personal information may be given out if required by law. If you test positive for HIV or if a CD4 or viral load is done at a study visit, by law we have to report the result to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. If hepatitis B and hepatitis C tests are positive, they will be reported to the local department of health.

HIPAA AUTHORIZATION
The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What personal health information is collected and used in this study and might also be disclosed?
The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, email address, dates directly related to you such as date of birth and clinic visits.
- Personal and family medical history
- Current and past medications or therapies
- Adherence questionnaires
- Results of tests and procedures you will undergo during this research
- Social Security Number, Medical record number

Why is your personal contact and health information being used?
Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?
The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

<u>Individuals or organizations responsible for administering the study:</u>

- ACTG Data Coordinating Center, Frontier Science Technology Research Foundation (FSTRF): Data for this study will be recorded on case report forms, keyed into a central database and electronically submitted to the Data Coordinating Center. The data will be cleaned and stored at this facility until it is ready to be analyzed.
- Statistical Data Analysis Center (SDAC): Approved data will be downloaded from FSTRF to the statistical data center for the AACTG at the Harvard School of Public Health. Specific study reports will be periodically provided to the study team and data safety review board to monitor if the trial is safe.
- Contract Research Organization (PPD, Inc): Monitors from PPD will visit the AACTG on a quarterly basis to review data and correct mistakes before the data are sent to SDAC for analysis.
- Government Agencies: Data from this study will be made available to the Food and Drug Administration and to the National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID), for them to evaluate the safety and efficacy of the treatments being used in this study.

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- Food and Drug Administration

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name, date of birth or medical record number. Information regarding your health, such as side effects of the study drug you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You must do so in writing to the Principal Investigator at Infectious Disease Division, 502 Johnson Pavilion Philadelphia PA 19104. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

What is an Electronic Medical Record?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What Are the Costs To Me?
There will be no cost to you for the study drugs, the study visits, physical examinations, laboratory tests or other tests required by the study. You or your insurance company, or your health care system will be responsible for the costs of your regular medical care as well as for the costs of drugs not given by the study.

Taking part in this study may lead to added costs to you and your insurance company if we learn of any medical problems that need extra testing or follow-up. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?
You will be compensated $50 for the required 11 study visits (screen, pre-entry, entry, Weeks 1, 2, 4, 8, 12, 18, 24 and 36) you attend, for a total of $550. In addition, you will be paid $25.00 for each FMD (arm ultrasound). There are 4 FMDs scheduled in the study (two ultrasounds at pre-entry, one at week 12, and one at week 24) for a total of $100 compensation if you complete all of the FMD study visits. If you are taking tenofovir (TFV) and you are one of the 21 evaluable subjects enrolled in a group and participating in the PK component, you will be paid $100 for the completed Week 2 PK visit. The payment for the PK part of the visit will be a check, which will be mailed to your home address about 4 weeks after the visit is complete. If you are required to come to the clinic for any additional visits, you will be compensated $35
There is no other form of compensation available such as reimbursements for parking, tokens or child care. In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

What Happens If I Am Injured?

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. The cost for this treatment will be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health. You will not be giving up any of your legal rights by signing this consent form.

What Are My Rights As a Research Subject?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. Your healthcare provider will treat you the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you want the results of the study, let the study staff know.

What Do I Do If I Have Questions Or Problems?

If you have questions about this study or a research-related injury, please contact the research team listed on page 1 of this consent form.

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

CONSENT

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

On page 3 of this consent form you were informed about optional tests to be done on your leftover blood.

If you agree, any blood left over after all required study testing is done may be stored (with no information that will identify you) and used for future ACTG-approved research. These blood samples may be stored for an unknown period of time. Results of testing done on these samples may not be given to you because they will be done in the future.

Please tick the box below to indicate your choice. You may change your mind at any time and reasonable efforts will be made to destroy your samples, though this may not always be possible.

☐ I agree to allow additional testing performed my extra samples for future ACTG-approved research

☐ I do not allow my extra samples to be used in future research

On page 6 of this consent form you were informed about an optional PK sample collection.

Please tick the box below to indicate your choice. You may change your mind at any time regarding participation.

☐ I agree to participate in the PK sample collection

☐ I do not want to participate in the PK part of the study

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date